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No. ~~11~~: A NEW CONCEPTION OF THE GLOMERULAR FUNCTION, BY PROFESSOR T. G. BRODIE

ON CHANGES IN THE GLOMERULI AND TUBULES OF THE KIDNEY ACCOMPANYING ACTIVITY, by PROFESSOR T. G. BRODIE and PROFESSOR J. J. MACKENZIE

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CROONIAN LECTURE: *A New Conception of the Glomerular Function.*

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(Lecture delivered June 15, 1911,—MS. received December 9, 1912.)

[PLATE 26.]

I have chosen as the subject of this lecture the physiology of the kidney, and more particularly the mode of action of one part of it, namely the glomerulus. In 1906, at the meeting of the British Medical Association in Toronto, I brought forward a new conception of the action of this very characteristic portion of the renal apparatus, and since that time have been accumulating a considerable mass of evidence by the light of which my theory can be criticised.

Very shortly after the discovery of the main details of the structure of the kidney, Ludwig, basing his ideas upon the then known structure, put forward his well-known theory that the glomerulus was a filter, and since that time all discussions upon renal activity have centred round this theory because it offered an explanation of the mode of action of one part of the mechanism upon hydrodynamic principles. The necessary corollary following from this assumption of filtration is that a considerable degree of absorption must be effected as the dilute filtrate travels down the tubule, and how excessively great this must be was first pointed out by Heidenhain.

If we consider the results obtained by the earlier workers upon the kidney, very many of them appear sufficiently well explained by the Ludwig theory, but as in the course of years a far stricter examination of the theory was attempted, several observations were made which proved very difficult to explain, and in many cases it was necessary to make such extensive and often contradictory assumptions that it became increasingly difficult to accept the theory. Of recent years evidence has been obtained in many directions which in my opinion conclusively proves that the glomerulus is not a filtering surface. It is not my object to-day to discuss this point in any detail. I may refer to my lecture delivered before the Harvey Society in New York in December, 1909, where a short summary of the facts for and against filtration is given, or to the excellent paper by Magnus, in the 'Handbuch der Biochemie,' where it is discussed *in extenso*. It will be sufficient for my present purpose if I indicate the chief reasons which led me

to conclude that the idea of filtration at the glomerular surface must be abandoned.

Perhaps the most striking piece of evidence is derived from the consideration of the concentration and constitution of the urines obtained during extremely free secretion. The evidence is quite clear that the main bulk of the water secreted by the kidney undoubtedly comes from the glomeruli. Hence the more rapid the flow of fluid from the kidney the more closely must that fluid resemble in constitution the fluid discharged from the glomeruli, since a much shorter time is then allowed to the cells of the tubules to modify it by absorption or secretion, and *if* filtration is the active process in the glomeruli this fluid ought to approximate more and more closely in composition to the blood plasma so far as the salts, urea and all constituents of the plasma other than proteins are concerned. But the dilute urine secreted after drinking copious amounts of lager beer,* or of water,† shows a constitution in salts widely different from that of the blood. Considering only the total concentration, as estimated by the depression of the freezing point, it is quite easy to obtain a urine with $\Delta = -0\cdot1^\circ$ C., and one as low as $-0\cdot075^\circ$ C. has been recorded.‡ To effect a change in concentration so extensive as this denotes, by filtration through a semipermeable membrane, would necessitate a pressure difference on the two sides of the membrane of at least 4000 mm. Hg, a pressure difference utterly out of comparison with the blood-pressure. Therefore to make such a result accord with the filtration theory, it becomes necessary to assume a most extensive reabsorption of the salts and other substances of small molecular size, a reabsorption on such an extensive scale and at such a rate as is, I think, entirely out of the question.

If, in the second place, we investigate the correlation between the blood flow and the rate of secretion, we find that while there is a general correspondence, in that increased urine flow is usually accompanied by increased blood flow, this is by no means a universal rule.§ I have frequently observed in kidneys in which there was at the start a fairly free blood flow and but slow urine secretion, a copious diuresis to come on without any change in the blood flow. Indeed on no less than five occasions I have seen a distinct decrease in the blood flow to occur as the diuresis commenced, and moreover in these experiments the volume of the kidney actually increased. In every direction we find that the urine flow does not vary strictly with the blood flow nor

* Dreser, 'Arch. Exp. Path.,' 1892, vol. 29, p. 303.

† Macallum and Benson, 'Journ. Biol. Chem.,' 1909, vol. 6, p. 87.

‡ Macallum and Benson, *loc. cit.*

§ *Cf.* Gottlieb and Magnus, 'Arch. Exp. Path.,' 1901, vol. 45, p. 223.

with the blood-pressure, as should be the case were filtration the essential factor in determining the volume of the urine discharged from the kidney.

In the third place we have very decisive evidence against the Ludwig theory in experiments designed to test the second assumption in that theory, namely that of reabsorption. If this is a process which occurs extensively within the tubules, and we bring into play any factor which favours reabsorption, we ought to effect a diminution in the volume of urine yielded by the kidney. Such a factor is an increase in hydrostatic pressure within the ureter, tending to prevent the outflow of urine. All that is necessary is to make the kidney discharge against a small pressure. The experiments carried out by most experimenters upon these lines have indeed yielded results which may be interpreted as indicating increased reabsorption. But we may urge as a general criticism against such results that the degree of decrease of urine flow is surprisingly small when we remember how essential it is according to Ludwig's theory to assume that reabsorption is excessively free. The kidney working against even a small hydrostatic pressure ought to show far greater reabsorption than was actually obtained. But the whole idea of reabsorption as an active process in the formation of urine has been completely disproved by Miss Cullis and myself,* for we were able to prove that decrease in rate of the urine flow when a kidney was made to secrete against a pressure was only a universal result when the animal was under an anæsthetic, and that if the animal were pithed and the experiment then performed in the absence of an anæsthetic, the kidney working against a small pressure always excreted more salt and usually more water than the opposite kidney.† The action of a pressure then tends to excite the kidney to greater activity, a result which entirely disproves the possibility of reabsorption being an extensive factor in the normal formation of urine.

Yet another point which militates greatly against the idea that the glomerulus is a filter is the behaviour of the kidney after temporary asphyxiation. If the renal artery be clamped for one minute and then released, the kidney does not at once begin to secrete, although the blood flow returns at once. It is only after a variable, but usually considerable delay that the kidney restarts, and at first the urine flow is very slow, only gradually returning to a rate comparable to the initial flow. If the artery has been clamped for any length of time the urine first collected after

* Brodie and Cullis, 'Journ. of Physiol.,' 1906, vol. 34, p. 224.

† Subsequent to these experiments I have found that, under the same conditions, the blood flow through the kidney is not altered by the small rise in ureter pressure employed in our experiments.

the re-establishment of the circulation contains protein, casts, even hæmoglobin, indicating considerable damage to the renal epithelium, either of the tubules or of the glomeruli or of both. But even if the glomerular epithelium be damaged it is inconceivable that this should temporarily abolish all the filtering properties it formerly possessed, and it is just as difficult to understand why the recovery of its power to filter should occur so gradually when the asphyxiation is arrested.

Let us next turn to the evidence that has been sought in favour of Ludwig's theory from experiments upon the maximum ureter pressure. One of the earliest attempts to associate the formation of urine directly with the blood-pressure was a measurement of the maximum height to which the kidney could force the urine up a vertical tube. As is well known, in the case of the salivary gland, the gland can secrete water to a pressure exceeding that of the blood in the carotid artery, a clear indication that a new force, viz., one exerted by the salivary gland cells, is at play in producing the result. But in the case of the kidney the result is very different. For the maximum ureter pressure always lies below the aortic blood-pressure, and usually some 30–40 mm. Hg below that pressure. The results were therefore interpreted by supporters of the filtration theory as indicating that as soon as the pressure within Bowman's capsule reached a point some 30 mm. Hg below the glomerular blood-pressure, filtration ceased, and Starling* explained the difference between the aortic pressure and the maximum ureter pressure as being the pressure difference necessary for the separation of the blood proteins from plasma, for he estimated the osmotic pressure of the blood protein at that amount. It has since been shown, however, that the protein osmotic pressure is certainly much less than this. Moreover Starling failed to allow for a loss of pressure between the aorta and the glomerular capillaries. Without doubt the loss of pressure between these points is less than in the case of ordinary capillaries, for the resistance in the kidney arterioles when dilated is certainly much less than at most points on the systemic circulation. As I shall show later, the maximum ureter pressure as ordinarily taken is a measure of the blood-pressure in the glomerular capillaries.

But a still more difficult problem is offered to those accepting the filtration theory in explaining these experiments. As was first pointed out by Heidenhain,† upon the Ludwig theory the maximum ureter pressure should be that pressure which just suffices to effect complete reabsorption of all the glomerular filtrate. Upon the theory we are to imagine an absorbing surface, capable of absorbing water, chlorides, urea and most of the bodies filtered in

* Starling, 'Journ. of Physiol.,' 1899, vol. 24, p. 317.

† Heidenhain, 'Hermann's Hdb.,' vol. 5, p. 327.

urine at a very fast rate. Such an absorbing surface would be influenced, as indeed is usually assumed by the supporters of Ludwig's theory, by a rise in pressure of the fluid at the surface. It then becomes very difficult to explain how the ureter pressure could ever be driven so high as is usually observed, especially when we remember that the rise in pressure can be effected with great rapidity.

Yet another result obtained in these experiments upon maximum ureter pressure is very significant. I have found that the maximum ureter pressure is practically the same whether the kidney be made to secrete a moderate amount of urine or a very large quantity. If reabsorption be a very active process, then the maximum ureter pressure in the latter case ought to be distinctly higher than in the former. As a matter of fact, it is not.

Taking everything into account, therefore, I have very grave doubts as to the occurrence of reabsorption in the tubules, and I am sure, if it does take place, that it is insignificant in comparison to that demanded by Ludwig's theory.

The Function of the Glomerulus.

Arriving then at the conclusion that the filtration theory was incorrect, I came back once more to the old problem: How are we to explain the very peculiar and characteristic structure shown by the glomerulus? I finally hit upon the idea that it was simply a means of utilising the blood-pressure for setting up a pressure head sufficiently great to drive the urine secreted at the glomerular surface down the tubule. To express this idea I term the glomerulus a propulsor. As is abundantly proved, the main volume of the water of the urine is secreted into the capsule of the glomerulus. To drive it from the capsule down the tubule requires a definite pressure-head. Whence is this pressure head derived? My view is that the intraglomerular blood-pressure is transmitted directly through the thin-walled glomerular loops to the fluid which has been secreted into the capsule, and thus a pressure is communicated to the fluid sufficient to force it down the tubule. To test this view, let us imagine that a certain amount of fluid has accumulated within Bowman's capsule. The problem then becomes: How is that fluid discharged down the tubule? If we know the number, length and lumina of the tubules, and the total amount of fluid leaving the kidney within a given time, it becomes easy to calculate the pressure-head which must have existed within each capsule in order to drive the fluid out of the kidney. It is simply an application of Poisseuille's law. I therefore performed two experiments upon the following lines. An active diuresis was established in an anæsthetised dog, and the rate at which urine was being discharged from one of the kidneys was determined. The pedicle of the kidney was

then ligatured and the kidney fixed entire in 10-per-cent. formalin solution. After fixation the whole kidney was cut into slices each about 7 mm. thick. The medulla was carefully separated from the cortex, and the latter collected and weighed. Next three small pieces of the cortex, selected from different regions of the kidney, were weighed separately. These were imbedded in paraffin and serial sections mounted. The sections were about 8μ thick. The next point was to determine the number of sections through which a single glomerulus extended. For this purpose ten glomeruli were followed through the series, and the mean number of sections through which one glomerulus ran thus ascertained. Lastly the total number of glomeruli in each section was counted, and the total number for all sections, divided by the average number for a single glomerulus, gave the total number of glomeruli present in that block of cortex. Similar calculations were made from each of the other two pieces. Then, knowing the weights of the three pieces and the total weight of the cortex, the number of glomeruli in the whole kidney was obtained.* The first dog weighed 11 kgrm., its right kidney weighed 34·5 grm., and the total number of glomeruli was 142,000. A kidney of a second dog, weighing a little over 8 krgm., contained 125,000 glomerali.

Employing a different method, Peter† calculated the number of glomeruli in the dog's kidney as 300,000. He does not give the weight of the kidney, nor does the method he employed appear to me comparable in accuracy with that above described. I have not been able to find any further record of enumerations of the glomeruli in the dog's kidney, and I wish to acknowledge my great indebtedness to Miss M. G. Thackrah for carrying out this very tedious piece of work.

Measurements of the lumina of the tubules in their several parts were now made, as also approximate estimates of the lengths of the tubules based upon the measurements of Peter.

The average results obtained from these measurements in the case of the first kidney were :—

	Length. cm.	Diameter. μ.
Proximal convoluted tubule	1·2	12
Loop of Henle —		
Descending limb	0·9	10
Ascending limb	0·9	9
Distal convoluted tubule	0·2	18
Collecting tubule.....................	2·2	16

* This is practically the method originally adopted by Huschke in 1828 ('Isis,' vol. 21, p. 550).

† Peter, 'Verhandl. D. Anat. Ges., Würzburg,' 1907, p. 120.

The diuresis at the time the kidney pedicle was ligatured was 1 c.c. per minute.

From the formula for the flow of liquids along narrow tubes

$p = 8l\eta/\pi r^4$ times flow in cubic centimetres per second dynes per square centimetre,

where l is the length of the tubule in centimetres,

η is the coefficient of viscosity, and

r is the radius of the tube in centimetres.

Taking η as 719×10^{-5}, the coefficient of viscosity of water at 35° C., we have

$$p = \frac{8 \times 719 \times 10^{-5}}{\pi} \cdot \frac{1}{60} \cdot \frac{1}{142000} \cdot 10^{16} \cdot \frac{l}{r^4} \text{ dynes per square centimetre,}$$

r being now expressed in microns; or

$$p = \frac{8 \times 719 \times 7}{22 \times 6 \times 142 \times 1333{\cdot}2} \cdot 10^{7} \cdot \frac{l}{r^4} \text{ mm. Hg.} = 1{\cdot}611 \times 10^4 \times \frac{l}{r^4} \text{ mm. Hg.}$$

Consequently, for a flow of 1 c.c. per minute,

	μ.	mm. Hg.
p per centimetre of tubule, when	$r = 4{\cdot}5$,	$= 39{\cdot}29$,
	$r = 5$,	$= 25{\cdot}78$,
	$r = 6$,	$= 12{\cdot}43$,
	$r = 8$,	$= 3{\cdot}93$,
	$r = 9$,	$= 2{\cdot}46$.

Hence pressure-head required for—

		mm. Hg.
Proximal convoluted tubule......	$= 1{\cdot}2 \times 12{\cdot}43$	$= 14{\cdot}916$
Loop of Henle—		
Descending limb	$= 0{\cdot}9 \times 25{\cdot}78$	$= 23{\cdot}212$
Ascending limb..................	$= 0{\cdot}9 \times 39{\cdot}29$	$= 35{\cdot}361$
Distal convoluted tubule	$= 0{\cdot}2 \times 2{\cdot}46$	$= 0{\cdot}492$
Collecting tubule	$= 2{\cdot}2 \times 3{\cdot}93$	$= 8{\cdot}646$
Total pressure-head.........		82·627

In the case of the second kidney, with 125,000 tubules, the measurements were :—

	Length. cm.	Diameter. μ.
Proximal convoluted tubule......	1·0	12
Loop of Henle—		
Descending limb	0·8	10
Ascending limb	0·8	10
Distal convoluted tubule	0·2	18
Collecting tubule	2·0	8

And, with a diuresis of 0·85 c.c. per minute, the pressure-head required works out to 74·1 mm. Hg.

I do not wish to lay too great a stress upon the actual pressure-head thus obtained, for the possible errors in the measurements are many. It is, for instance, impossible to obtain anything but an approximation to the lengths of the successive portions of the tubule, and also the measurements of their lumina can only be approximate, for they are undoubtedly altered during fixation. Also I have supposed all the tubules to have equal lumina, and have neglected to take into account those tubules which were at rest. To obtain the total pressure within Bowman's capsule a factor for the velocity head should be added to the pressure-head already calculated, but it is so small that we may omit it. (The mean velocity within the narrowest portion of the tubule amounts to about 1 mm. per second.)

The important point is that during an active diuresis a pressure-head of the order of 80 mm Hg. may be needed within Bowman's capsule to drive the fluid secreted there down the tubule.

The mean aortic blood-pressure in the first experiment was 120 mm. Hg. and in the second 115 mm. If we allow 30–35 mm. Hg as the loss of pressure-head between the aorta and the glomerular capillaries when the afferent glomerular vessels are dilated, the blood-pressure within the capillary loops would amount to 90–85 mm. Hg in the first experiment, and 85–80 mm. in the second. Hence, on these figures, practically the whole of the blood pressure-head is required to set up a pressure-head in the fluid within the capsule sufficient to drive the secreted fluid down the tubule. Bearing in mind that the estimates given are only approximate, I conclude that the pressure-head within Bowman's capsule only differs from the pressure-head within the glomerular loops by the pressure required to stretch the walls of the loops. This latter probably does not amount to more than one or two millimetres of mercury.

If in the light of these arguments we criticise once more the assumptions made by Ludwig's theory, we see that that theory becomes less tenable than ever. In the first place, when the kidney is secreting water at its fastest rate, the pressure difference available for filtration is reduced to a minimum. At lower rates of secretion, of course, a pressure difference might be available. In the second place, the assumption must be made that the volume of water discharged from the glomerulus is from 30 to 70 times greater than the volume of water entering the pelvis of the kidney. Hence a very much greater pressure-head would be required to drive that fluid down the tubule, though not 30 to 70 times greater than the pressure required to drive a volume equal to that of the discharged urine, since the fluid has to be driven only as far as the absorbing surface. But as the absorbing surface would have to be taken as extending at least to the end of the ascending limb of

the loop of Henle, *i.e.* along considerably more than one-half of the whole tubule, and the whole length of the narrowest part of the tubule, the pressure-head required would be enormous, certainly many times greater than the glomerular blood-pressure. We should, therefore, be compelled to ascribe to the cells secreting the water the power of setting up a very high hydrostatic pressure, and all the evidence is strongly against any such view. A pressure within Bowman's capsule greater than the blood-pressure would at once lead to the closure of the glomerular loops and arrest of the circulation. This is the main reason why neither the cells of Bowman's capsule, nor those covering the glomerular tufts, nor those of the convoluted tubule, possess the power of setting up a hydrostatic pressure.

The quantity of energy imparted by the blood to the glomerular secretion is only a small percentage of its total amount. Thus if V be the minute volume of blood flowing through the glomerulus, and v the minute volume of glomerular secretion, then V c.c. of blood enter the glomerular capsule, and $V-v$ c.c. leave it. If p be the pressure-head in the glomerular loops, the pressure energy of the blood entering is Vp, and that of the blood leaving is $(V-v)p$. The pressure energy communicated to the glomerular secretion is vp, and the ratio of this to the total pressure energy of the blood as it enters is v/V. In the dog's kidney V may have any value from 200 to 600 c.c., and v from 1 to 2 c.c. at the height of a diuresis. Thus the pressure energy given up by the blood lies somewhere between 1 and 0·16 per cent. of its total pressure energy.

Histological Evidence.

In the next instance the test applied was that of microscopical examination of the kidney after varying degrees of activity. If during diuresis fluid is being forced at a considerable pressure from Bowman's capsule down the tubule, evidences of the action of this pressure should be indicated by changes both in the glomerulus and in the tubule. It is very remarkable that throughout the literature the accounts of changes in the glomerulus following activity are so scanty, and many authors state that no changes whatever are to be found (*e.g.* Lamy and Mayer). Mackenzie and I therefore examined a number of kidneys excised after diuresis had been induced under various conditions, and found that decided changes are produced in the glomerulus and tubule. We further found abundant evidence proving that the tubules have been subjected to a high internal pressure. The full details of these changes are given in a separate paper.* The general results are as follows:—

On comparing a resting kidney with one that has been thrown into activity

* *Vide* p. 593.

by the injection of any diuretic which causes a free flow of water, the differences between both glomeruli and convoluted tubules are of the most striking character. These differences are illustrated in figs. 1 and 2 which show the changes in the cortex under a low magnification. The important points are the following:—In an active kidney the glomeruli are always separated from the capsules, and usually there is a considerable accumulation of fluid in this position. The capsule is always rounded whereas in the resting kidney the capsule lies in contact with the glomerulus and the whole structure is usually irregularly polyhedral in shape. In an active kidney, in contradistinction to the resting, the individual loops of the glomerulus are frequently separated from one another and stand out clearly. The glomerulus also has a very characteristic vacuolated appearance, due, we think, to dilated capillaries, from which the red blood corpuscles have in some way or other been removed or destroyed, possibly *post mortem*. When examining two such kidneys under a low power of magnification the contrast is most striking. In the resting kidney the glomeruli are far from conspicuous, and have to be sought for. In the active kidney, on the other hand, they stand out at once as the most conspicuous objects in the field of view.

The changes in the tubules are just as striking. Whereas a resting proximal convoluted tubule possesses no lumen, one in activity has a large lumen. This is true both of the proximal and the distal tubules. Moreover, in the resting kidney the tubules are very much twisted on themselves and form very complicated foldings, whilst in the active kidney the appearances indicate that the tubule is as far as possible straightened out. All these several points prove quite clearly that the tubules have been subjected to some high fluid pressure from within.

The changes accompanying activity are strikingly emphasised when we measure the diameters of these several structures. In the case of the glomeruli and capsules, in addition to measurements in diameters at right angles to one another, approximate calculations of their volumes were also made.

In one experiment which we may take as typical we obtained the following results:—

	Resting.	After activity.
Volume of capsule...........	83*	220
" glomerulus	80	111
" fluid in capsule	3	109

* These figures can be converted into cubic millimetres by multiplying them by $4 \cdot 2 \times 10^{-6}$.

The differences are therefore very great. The capacity of Bowman's capsule in the active kidney is nearly three times that of the capsule in the resting kidney, chiefly on account of the big accumulation of fluid within the capsule.

The volume of the glomerulus has also increased, though only by 40 per cent. Such measurements prove, therefore, that both the glomerulus and the capsule of Bowman are extensible structures, and that a considerable volume of fluid accumulates in the capsule during activity.

In drawing deductions from these measurements, full attention must be paid to possible alterations occurring after the kidney is excised. To obviate change as far as possible in these experiments, the artery, vein and ureter were ligatured close to the hilum at the instant the experiment was to be stopped, using a single coarse ligature. The kidney was then excised, rapidly weighed, and placed at once in the formalin fixative. If active diuresis were in progress, the kidney at the moment of ligature was hard and tense, but within a few seconds after application of the ligature became quite soft, chiefly on account of escape of blood through the Capsule. We found it impossible to avoid this. The question therefore arises: Does this fall of tension within the kidney substance involve a change in distribution of the fluid contained within the tubule and capsule? It is possible, for instance, that fluid is forced back from the distended tubule into the capsule. Possibly this may be the cause of some of the increase in volume of the capsule seen in our experiments, but the changes are too great to be wholly, or even largely, explicable in this way. There is yet another *post-mortem* change we think possible, viz., that before the fixative has time to penetrate and reach the glomeruli, the cells forming the loops die and permit osmotic effects to take place through them between the fluid in the capsule and the blood. Fluid would pass into the blood, and we think it possible that this fluid is so low in salinity as to lake some of the corpuscles, thus producing the vacuolated appearance described above.

In the same experiment the measurements of the diameters of the proximal and distal convoluted tubules and of their lumina were as follows:—

	Resting. μ.	Active. μ.
Proximal convoluted tubule—		
Transverse diameter	44·0	43·0
Lumen, diameter	0·0	19·4
Distal convoluted tubule—		
Transverse diameter	25·4	31·8
Lumen, diameter	11·0	21·8

This is fairly typical of the results obtained in all our experiments. We found it to be practically a universal rule that the external diameter of the proximal convoluted tubule remained unaltered, or showed but a slight increase or decrease. The marked change during activity is the production of a big lumen within the proximal tubule. The idea given by an examination of the sections is that the loops of the convoluted tubule have been opened out and stretched in length. They are in nearly all instances circular in outline, and invariably, as just stated, there is a very wide lumen. The distal convoluted tubule in contradistinction is nearly always increased in diameter in the active state, and the lumen greatly increased, often doubled, although this tubule has invariably a rather large lumen even in the resting kidney.

We have not yet carried out a sufficient number of measurements of the remaining portions of the tubule to warrant us making any decided statement as to the changes they undergo. It is clear that the limbs of the loop of Henle are both distended, and often the collecting tubules show very distinct expansion.

The next modification in our experiments consisted in comparing the two kidneys after active diuresis, one kidney having been previously stripped of its Capsule.

The kidney is very characteristically enclosed in a strong and practically inextensible Capsule*, and my view of the meaning of the glomerulus offers an explanation of that fact. As fluid is secreted into Bowman's capsule by the epithelium covering the glomerular loops, and possibly also by the epithelium of the capsule, the blood-pressure acting within the glomerular loops is transmitted directly to that fluid and through it to the wall of Bowman's capsule. This latter, as we have seen, is extensible and might be ruptured if the distension were carried too far. Again, fluid is at once forced into the convoluted tubule, and that also might be ruptured if overdistended. To prevent any dangerous overdistension the whole of the structures are enclosed in a firm Capsule. That this distension does take place on activity is amply proved in a variety of ways. Firstly, as shown above, the histological appearances demonstrate it. Secondly, if in an experiment we excise one kidney at the commencement, then excite diuresis, and at its height ligature the pedicle of the other kidney to prevent escape of urine from the tubules, and we then weigh the two kidneys, the latter often shows an increase in weight amounting to about 30 per cent. This increase in weight is not due to blood, for on excision the blood escapes more readily from such a kidney than from a

* In order to avoid confusion between the Capsule of the kidney and Bowman's capsule, I will when referring to the former distinguish it by a capital.

resting kidney. In the third place I have often observed the following changes during the course of an oncometric experiment viz., a large increase in the volume of the kidney, a free flow of urine, but a decrease in the rate of blood flow through the kidney. Here the plethysmographic increase is due to an accumulation of urine within the capsules and tubules. Lastly, if we examine a kidney at the height of a diuresis we always find it very hard and tense. The Capsule is distended to its fullest degree. If we attempt to make such a kidney expand still further by temporarily clamping the vein we fail completely. We see then that some of the tension set up by the blood-pressure in the glomeruli is transmitted through the capsule wall and the walls of the tubules to the general renal tissues. How much pressure is thus transmitted depends upon the resistance to distension offered by Bowman's capsule and the walls of the convoluted tubules. Their structure, particularly that of the capsule, indicates that they probably offer a fairly considerable resistance. We could get an estimate of this by finding the difference between the blood-pressure in the glomeruli and the general tension of the kidney substance within its Capsule. I made some attempts to measure this latter during active diuresis, but at present have not obtained any very accurate results. As far as they go they indicate a tension of about 40 mm. Hg.

If this be the true meaning of the kidney Capsule then, if we remove it before exciting diuresis, the kidney ought to expand still further as compared to the intact one, and the amount of that further expansion should depend upon the general rigidity of the kidney substance and the amount of connective tissue it contains. Our experiments proved this to be the case. The weight of such a kidney compared to one with the Capsule untouched was always greater, especially in the rabbit's kidney. In the cat there are a number of incomplete septa running transversely towards the hilum, and on active diuresis the kidney substance bulges notably between these, giving the appearance of constricted grooves in the bottom of which veins run. This relatively greater increase in volume of the kidney as a whole is also found in the several parts of the tubule, and when we measured the tubules and glomeruli in such kidneys, the differences were very distinct. For instance, in one experiment the right kidney was untouched, and the left decapsulated. The following approximate volumes of the capsule and glomerulus after diuresis were obtained:—

	R.	L.
Volume of capsule	205	257
,, glomerus	128	151
,, fluid	27	106

The diameter of the tubules was as follows:—

	μ.	μ.
Proximal convoluted tubule—		
External diameter	44·8	48·0
Lumen	13·0	19·8
Distal convoluted tubule—		
External diameter	33·2	39·2
Lumen	24·8	29·2

The expansion then is found in all parts, and is obviously brought about by a distending force acting within the tubules.

Yet another means of testing the theory which presented itself was to observe the effect of obstructing the exit of urine down the ureter. In the first set of experiments a diuresis was set up, and at its height the ureter on one side was suddenly clamped. Five to fifteen minutes later the two kidneys were exposed, their condition noted, and then the pedicles ligatured as close as possible to the hilum. The kidneys were then removed and weighed. As was to be expected, a kidney obstructed in this manner is very distended and tense within its Capsule. The weights found in one experiment in which the right kidney was obstructed at the height of diuresis, and the left secreting freely, were as follows:—

	grm.
Weight of R. kidney	15·5
" L. kidney	13·5

The right kidney was very tense, appeared almost bloodless, and was distinctly lobulated. The left kidney was distinctly softer than the right and also more vascular. The approximate volumes of the capsules and glomeruli were:—

	L.	R.
Volume of capsule	86	146
" glomerulus	69	89
" fluid	17	57

The measurements of the tubules were:—

	μ.	μ.
Proximal convoluted tubule—		
External diameter	39·2	39·4
Lumen	6·6	14·0
Distal convoluted tubule—		
External diameter	22·8	28·2
Lumen	12·6	18·4

Lastly, in an experiment in which an obstructed kidney was compared to a decapsulated one we found that the former procedure produced more effect than decapsulation.

Maximum Ureter Pressure.—Another series of observations which receive a satisfactory explanation is that in which the maximum ureter pressure is measured. According to my theory, fluid should be forced out of the tubules only when the pressure within the ureter lies below the maximum glomerular blood-pressure. This of course assumes that the tubular epithelium in secreting does not set up any appreciable hydrostatic pressure. From this point of view the measurement of the maximum ureter pressure should be a means of determining the intraglomerular blood-pressure, always supposing that none of that pressure is taken up by the walls of the glomerular loops. Now the measurements of the maximum ureter pressure fit in perfectly with this conception. In an animal whose aortic blood-pressure is about 120 mm Hg, the maximum ureter pressure is usually found to be somewhere between 80 mm. and 90 mm Hg, that is, a loss of pressure-head of some 30 to 40 mm. Hg occurs between the aorta and the glomerular capillaries This is distinctly less than is the case for most systemic vessels, and fits in well with our knowledge of the relatively wide and short path of the blood stream from the aorta to the glomerulus. We have only to recall how fast the blood may flow through the kidney to realise that the glomerular capillary pressure during activity must stand at a greater height than the ordinary systemic capillary pressure.

Let us then return to a general restatement of the whole problem. I have given evidence that the glomerulus, Bowman's capsule and certain parts of the tubules are elastic structures, and that their overdistension is prevented by the general inextensibility of the connective tissue framework and of the Capsule. Consequently as soon as fluid is secreted by the glomerular surface into the capsule, the glomerular capillary pressure comes into play, and some part of that pressure is transmitted through Bowman's capsule to the tubules immediately outside. Then as the secretion continues to accumulate, the kidney expands to fill the Capsule, and the pressure within the Capsule reaches its maximum. Hence we may regard the glomeruli as a number of expanding vascular tufts, lying within a space which cannot expand beyond a certain point, consequently the expansion of the glomeruli expels any fluid free to move outwards. It is as if we were dealing with a sponge work filled with fluid, and enclosed in a capsule which it completely fills. Distributed through the sponge are a number of elastic structures which can be expanded by a fluid pressure acting from within, their expansion necessarily compressing the sponge, *i.e.* expelling the fluid from between its interstices. This analogy

is of course incomplete, in that it takes no account of the tubular structure, and the facts that the pressure is set up in the fluid within the tubules and that the walls of the tubules offer some resistance to expansion. The first effects of the glomerular pressure will therefore be to distend the capsule and the first convoluted tubule, *i.e.*, to increase its lumen, thus offering less resistance to the flow of fluid along the tubule. In this distension the pulsation of the glomerular vessels is probably utilised. Also the more rapid the flow along the tubule the greater the pressure gradient, and the smaller the pressure transmitted through the walls of the tubules to the general kidney substance. We must therefore expect to find a distinct difference between the intratubular pressure and the intra-Capsular pressure, and while fluid is moving down the tubule the two could only be equal at the point where the tubule leaves that part of the kidney substance where the pressure is raised. This region is limited as we shall see by the branching arches of the renal vessels in the intermediate zone.

There is yet another feature of the renal structure and form which is capable of interpretation by this theory. This is the general shape of the mammalian kidney, so typical as to give its name to all structures in any way resembling it. The kidney is very typically constructed of a cortical mass enveloping a medullary portion. The blood-vessels form a set of arches between these two parts. My suggestion is that this arched system of vessels forms a more or less rigid base upon which the cortex lies. Consequently when, in activity, the pressure in the general renal tissue rises through the activity of the glomeruli it is restricted in the first instance to the cortex. The cortex, so to speak, becomes compressed between the rigid Capsule and the firmly distended arterial arches. From this general pressure the medullary portion is relieved, and it is a most significant fact that the loops of Henle lie within this region, where there is probably but little external pressure. Apparently, then, the difference in state between the tubules in the cortex and those in the medulla is that there is a high pressure on both internal and external surfaces of the tubules lying in the cortex, whereas in the medulla the pressure may be acting chiefly, possibly entirely, from the inner surface of the loops only. In this connection I have frequently observed the following most notable result:—If at the height of a diuresis whilst urine is flowing freely the ureter be ligatured, and after about 20 minutes the pedicle be tied off and the kidney removed, it will be found that the pelvis is widely distended with fluid, and usually the pyramid is compressed towards the cortex until it forms an almost insignificant structure projecting into the cavity of the pelvis. Histo-

logically the tubules within such a collapsed pyramid are observed to be flattened and empty.

It is possible that some or even all of this compression might be *post mortem*, but I think that it is *ante mortem*, since it is only found if sufficient time be allowed to lapse between the ligaturing of the ureter and the removal of the kidney. The longer the interval the more marked is the compression. I think the compression is produced in the following way:—After the ureter has been ligatured urine continues for a time to be expelled into the pelvis, and gradually the pressure there rises. Fluid will continue to be forced into the pelvis in gradually decreasing volume until the pressure reaches that of the glomerular capillary blood-pressure. The further distension of the pelvis and compression of the medulla is probably produced through the pulsatory variations of pressure in the cortex. The systolic pressure, by the expansion of the glomeruli and arteries, suddenly raises the tension throughout the whole cortex, thus expels a little of the fluid from the terminal portions of the tubules into the pelvis, whose pressure then becomes greater than diastolic pressure. As the pressure falls in diastole a point is reached at which the cortical pressure is below the pressure in the pelvis, that is below the pressure in the fluid contained within the loops of Henle and the collecting tubules. Accordingly these latter are emptied or partially emptied into the cortical tubules, while the lower ends of the collecting tubules are compressed and act as valves, preventing any return flow from the pelvis up the tubule. In this way more and more fluid is gradually collected within the pelvis at the expense of the medulla.

If, as I think is the case, we may divide the kidney substance into two parts, in one of which the whole tubule is exposed to a considerable pressure, both internal and external, while in the other region the pressure is largely within the tubule, the difference must have some important physiological meaning. It is most significant that the loops of Henle are carried down into this region of low external pressure. In different animals the loops of Henle show many diversities of form, more particularly in length, and it is certainly a striking fact that in some animals the major number of loops are short, and either lie completely within the cortex or only descend into the outermost portions of the medulla. It has been pointed out that the animals with very short loops are those which secrete a dilute urine, whilst those in which the loop penetrates far into the medulla secrete a concentrated urine. Hence it may be that this loop effects a certain amount of absorption, a function which would be aided by a pressure difference acting from within the tubule.

To test my theory further, and in the hope of gaining some evidence of the

respective activities of the different parts of the renal apparatus, another series of experiments was performed, in which the action of diuretics upon animals whose blood-pressure had been lowered by section of the spinal cord was tested. It was necessary to employ rabbits for these observations, since in both the cat and the dog the blood pressure remains high enough after section of the cord to enable the kidney to secrete quite freely when a diuretic is administered. In the rabbit the blood pressure falls to about 30 mm. Hg. and even though we injected large doses of saline and other diuretics we never obtained a single drop of urine from the kidneys. The plan of experiment therefore was to excise one kidney some 10 to 20 minutes after division of the spinal cord, then inject the diuretic to be studied, and half-an-hour later to remove the other kidney. In this way evidence was obtained indicating the point of action of various diuretics. Without going into the results in detail, I may state that the glomerulus is excited to secrete by most of the diuretics of the saline group. This activity was well marked after sodium sulphate, urea or dextrose; it was excited also by caffeine but completely absent after phloridzin. In the tubules the results were equally striking, especially in the case of phloridzin, and in a minor degree in the case of caffeine. In no instance was a large lumen produced, and the external diameters of the convoluted tubules were only slightly increased. The contents of the lumen consisted of fairly large secretion droplets, the droplets being enclosed in membranes which stained with Weigert's hæmatoxylin, and fairly well with eosin. These results were chiefly observed in the proximal convoluted tubule. With the low blood-pressure there was never the slightest indication of any marked distension of the tubule in any part of its course. The glomeruli were never found secreting very actively, but were always found separated from the capsular epithelium by a distinct though small accumulation of fluid.

An examination of the embryology of the renal tubule bears out the views I have expressed. Originally, the excreting apparatus was a long tubule opening at one end into the body cavity and at the other on to the surface. This tubule was lined throughout by a ciliated epithelium, which provided the necessary motor mechanism for the expulsion of the secretion. Later, the glomerulus was developed from the dorsal wall of the body cavity and received a large and important blood supply from the aorta. Possibly its original function was to secrete a watery fluid into the body cavity, and this in some way served the renal tubule. The arrangement of its vessels as large loops projecting from the cœlomic wall, even at this early stage, tends to indicate that it was employed as a means of raising the fluid pressure within the

cœlom. In the next stage of development that part of the body cavity which contained the orifices of the renal tubules and the glomeruli became largely constricted off from the rest, and by means of imperfect septa the glomeruli also became partially separated from one another. This indicates that the function of the glomerulus has now been restricted almost solely to work in association with renal excretion. Later, this becomes entirely the case by the complete separation of that portion of the cœlom from the rest. Each glomerulus then works in conjunction with a renal tubule, but at first the number of the latter is largely in excess of the former. The material secreted at the glomerular surface is now conducted entirely to the tubule, as is also any formed by the isolated portion of the cœlomic endothelium. It is very significant that as soon as the relationship between glomerulus and tubule is completed the latter loses its cilia, only the cells of the neck of the tubule retaining them in some animals. This indicates that some other mechanism for the propulsion of fluid down the tubule has taken the place of the ciliary movement. This, according to my view, is the propulsive action of the glomerular capillary loops.

Previous Work Bearing upon the Subject.

L. Hill, in discussing the general distribution of pressure through a soft and yielding animal tissue arrives at the conclusion that filtration is an impossible mechanism at the glomerular surface. With much that Hill expresses in his paper on "Filtration in the Living Organism,"* I am in complete agreement, but in several points I think he is [illegible]. Thus, he considers that the glomerular capillary pressure must be transmitted in undiminished amount throughout the whole renal tissue. This implies that the wall of Bowman's capsule is incapable of offering any resistance to extension, and similarly, too, for the walls of the tubule. Our measurements show, however, that while these structures expand, they offer resistance to expansion. They indicate that a higher pressure has been acting on the internal surface of the tubule than on the outer, and especially until a sufficient dilatation has been produced to make the kidney substance as a whole expand, and thus render the Capsule tense. From that point on, the tension in the kidney substance rapidly rises. I have found by measurements of the blood flow that at this point the blood flow falls, due, that is, to compression of the capillaries around the convoluted tubules and of the renal veins. The fact that the capillary system which originates this pressure consists of characteristic tufts which lie entirely within capsules is very significant. In certain forms of tubular nephritis, in which the

* 'Biochem. Journ.,' 1906, vol. 1, p. 55.

tubules are blocked or obliterated, and have been so for a considerable time, the capsules are often found distended to a volume even ten times greater than the normal volume. In these cases the glomerulus is collapsed and shrunken to a minute structure, which appears as a mere projection into the swollen capsules.

In my opinion, too, Hill does not allow a sufficient fall in pressure-head between the glomerular capillaries and the tubule capillaries. The efferent blood-vessel of the glomerulus is of small diameter and fairly long. Hence with the exceedingly rapid blood flow observed during diuresis, there must of necessity be a considerable pressure difference between these two capillary systems. I cannot, therefore, agree with Hill's statement: "The pressure of the secretion cannot be normally greater than the pressure *in* the veins, for otherwise the secretory pressure would compress the veins"; nor, again, with the statement: "The secretion moves onward, I take it, by phenomena of adsorption."

At about the same time Filehne and Biberfeld* reasoned that filtration at the glomerular surface was an impossibility, since there were no firm supporting structures capable of resisting any pressure. They, too, consider that the glomerular capillary pressure is at once transmitted through the whole renal substance, leaving no pressure difference available for filtration through the glomerular surface. While agreeing with them that but a very minute pressure difference can exist between the glomerular blood-pressure and the pressure of the secreted fluid within Bowman's capsule, I am in disaccordance with them, for reasons already stated, in their idea that the glomerular pressure is at once transmitted in undiminished amount to the general renal substance.

Shortly after I had expressed my views as to the work of the glomerulus, Lamy and Mayer† published a paper in which they suggested that the glomerulus by its pulsation acted as a kind of heart, and by its piston-like movements drove the liquid forward in the tubule, and favoured its discharge by overcoming the friction and the capillarity of the tubule. They do not consider that the glomerulus plays any important part in the secretion of water. If it secretes any at all, this is in their opinion quite a minor rôle. According to them the glomerulus performs mechanical work solely by virtue of its pulsation, and consequently their view differs widely from mine. I am, in the first place, in wide disagreement with them in that I consider that the main bulk of the water is secreted by the glomerular surface. There is abundant evidence to prove this. I need only refer to the work

* 'Pflüger's Archiv,' 1906, vol. 111, p. 1.

† 'Journ. de Physiol.,' 1906, vol. 7, p. 660.

of Miss Cullis upon secretion in the frog's kidney,* or to the results I have briefly described above upon secretion in the rabbit's kidney after division of the spinal cord. As is seen from what I have stated, the fact that the glomerulus pulsates has but little bearing, if any, upon its work in propelling the secreted water along the tubule. That pulsation is unimportant in the propulsor action of the glomerulus is borne out by the fact that the urine flows quite freely along the ureter of an excised kidney perfused with fluid at constant pressure, and if in these cases the perfusing fluid be of correct composition, the kidney presents at the end of the experiment appearances exactly comparable to those found by Mackenzie and myself after active diuresis in the intact animal. It is possible that pulsation may play a part in producing the primary dilatation of the convoluted tubule. In an artificial schema representing the glomerulus and tubule, I have found that the volume of fluid driven along the capillary tube by a pressure made to vary in imitation of the pulse variations is exactly the same as if a steady pressure at the mean height of the varying one is used. This indeed was to be expected from theoretical reasons. The value of a varying pressure only arises when the tubule along which the fluid is to be driven has first of all to be expanded.

In conclusion, then, we may summarise what I have said in the following way:—

The glomerulus is a secreting surface whose chief function is to secrete the main bulk of the water of the urine, but it is also thrown into activity by such substances as salts, urea, dextrose and caffeine. Its highly characteristic shape is to enable it to act as a means of setting up a pressure-head sufficient in amount to drive the secreted water down the long urinary tubule. The pressure originating from this is also transmitted in some degree through Bowman's capsule to the general tissues of the cortex, thereby exerting a pressure upon the external surfaces of all the tubules lying in the cortex. To what degree the pressure on the external surfaces of the convoluted and other tubules lies below the glomerular capillary pressure I am not yet able to state definitely. The fact that the convoluted tubules show such marked evidences of having been subjected to a high internal pressure certainly indicates a considerable diminution. I have also given reasons for believing that the general pressure conditions so typical of the cortex are non-existent in the medulla: there, apparently, the internal pressure acts upon the loops of Henle in undiminished amount, and must be supported either by the basement membrane of those tubules, or by the general tissue of the medulla itself. At present the former seems the more probable. Lastly I have given evidence attained by the application of yet another method, which enables us

* 'Journ. of Physiol.,' 1906, vol. 34, p. 250.

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to determine from histological evidence the part of the urinary apparatus thrown into activity by the different urine exciting substances.

[*Addendum.*—Shortly after I delivered this lecture before the Royal Society, letters appeared in the 'Lancet' and the 'British Medical Journal' by Mr. Wm. Woods Smyth, claiming that his brother, Dr. A. W. Smyth, had over 30 years ago anticipated the views I now expressed. Dr. Smyth's views of the function of the kidney appeared in a pamphlet by Mr. John Gamgee, in the 'New Orleans Medical and Surgical Journal' for May, 1880, and were based upon microscopic examination of the kidney, and upon the fact that the kidney pulsated with each heart-beat. As far as I am aware, no reference to his views has ever appeared in the literature upon the kidney. They concerned the glomerulus and the circulation through the kidney. He denies the existence of any "connection between the capsule of the Malpighian body and the interior of a uriniferous tubule," and also "having observed that the hyaline membrane, enclosing each glomerule, was unprovided with epithelium, essential to every secreting structure, Dr. Smyth perceived that so delicate a sac would rupture, and the plexus be destroyed, if subjected to hydrostatic pressure, either during secretion or from accidental regurgitation." But the main point in relation to this lecture is his view of the mode of working of the glomerulus. This he describes in the following terms:—"Every heart-beat is attended by turgescence of the glomerule. The loops, from their position and form, must swell outward and inward in all directions, and, constricting the efferent vessel, momentarily impede the blood's exit. At each cardiac diastole, the arterial column sustaining the blood in its channel, the Malpighian loops recoil and fill the current in the secreting vascular rete. And this is Dr. Smyth's view of the special function of the Malpighian bodies. Their alternate turgescence constituting a 'rhythmic vascular impulse,' a uniform, safe, and sufficient expelling pressure is maintained on the coiled tubes, and, indeed, on the whole excreting structure of the kidney. Those acquainted with the laws which govern the flow of liquids can readily understand that the power required to maintain a circulation, beyond the coils of the glomerule, would be destroyed, if a mere physical transudation could occur through the loops, so well disposed to bring the very active pulsation to bear on the maintenance of a circulation."

"The unmistakable constriction of the efferent vessel, on the filling of each glomerule, causes an alternation between clearance of the tubuli and the flow of blood in the secreting vascular rete. The glomerules are filled during the heart's systole; the secreting rete is turgid during the heart's diastole."

Undoubtedly Dr. Smyth's conjecture was in the right direction, but his erroneous conclusion that Bowman's capsule did not open into the tubule, and the fact that he ascribed all the expelling power of the glomerulus to its pulsation, will indicate sufficiently the great divergence of his views from those I have expressed in my lecture.]

DESCRIPTION OF PLATE.

Fig. 1. Microphotograph of Cortex of Kidney of Cat, after period of rest, showing absence of lumen in convoluted tubules and irregular outline of glomeruli. ×120.

Fig. 2. Microphotograph of Cortex of Kidney of Cat, after sulphate diuresis, showing widely dilated tubules and distended capsules, which are now rounded and contain much fluid. The glomeruli are larger than in the resting kidney, but not filling the capsules. ×120.

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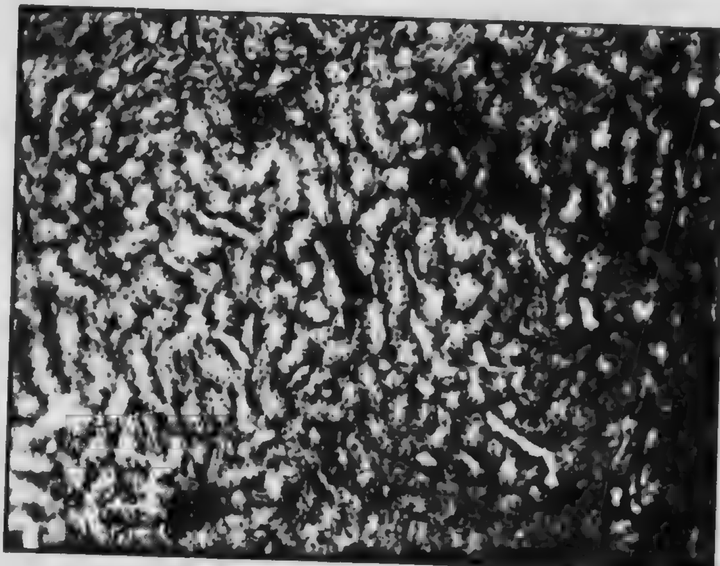

FIG. 1.

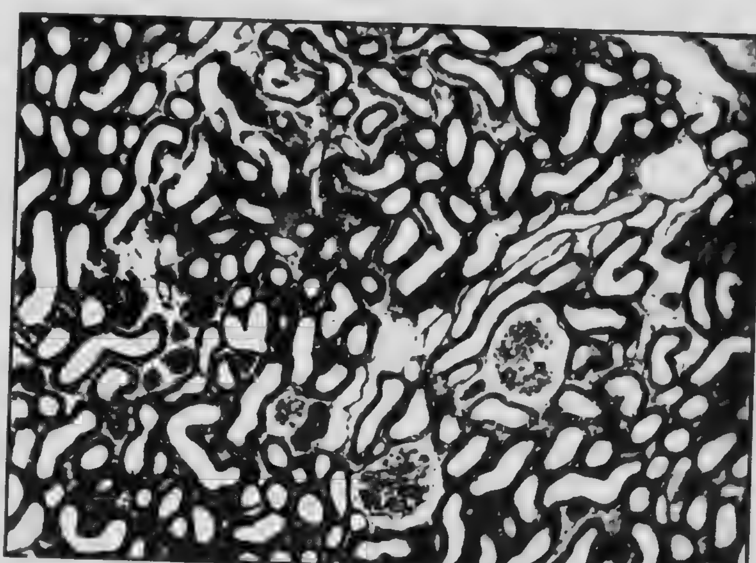

FIG. 2.

[*Reprinted from the* Proceedings of the Royal Society, B. Vol. 87]

On Changes in the Glomeruli and Tubules of the Kidney accompanying Activity.

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(Received December 9, 1912,—Read February 20, 1913.)

(From the Physiological and Pathological Laboratories of the University of Toronto.)

[Plate 27.]

The experiments described in this paper were designed to test the correctness of the view put forward by one of us,* namely, that the glomerulus is a propulsor. If this view be correct, the marked dilatation of the tubules, which is so prominent a feature in a kidney after active diuresis, is simply the expression of the forcible distension of the tubule from within, effected by the discharge of fluid from the glomerulus down the tubule, the active propelling and dilating force being the intraglomerular blood-pressure transmitted through the glomerular capillary cells and epithelium. As, however, the condition of the glomerulus after active secretion has not been made the subject of extensive observation, it seemed probable that a thorough study of the alterations in size and appearance of both tubule and glomerulus might give many points of importance in criticising the propulsion theory. Thus, if the capsule be free to expand, we may find it enlarged after active diuresis; and again, if the propulsive action of the glomerulus is complete and instantaneous, we should find the glomerulus filling Bowman's capsule completely under all conditions. But it was also possible that, after a very free secretion of water, there might be a considerable accumulation of fluid between the glomerulus and the capsule wall. We therefore measured the sizes of the capsules, the glomeruli and the tubules in kidneys, before and after diuresis had been set up under varying conditions. The more important of these states were:—

1. The kidney at rest.
2. The kidney secreting freely. This we term an "active free" kidney.
3. Decapsulated and secreting freely. This we term an "active decapsulated" kidney. The aim of the procedure was to test the explanation offered by the theory as to the meaning of the Capsule.†

* *Vide* Croonian Lecture, *supra*.

† As in the course of this paper we shall be referring constantly to the Capsule of the kidney and to Bowman's capsule, we will, in order to avoid needless repetition, distinguish between them by employing a capital letter whenever we refer to the former.

4. With the ureter ligatured. This we term an "active obstructed" kidney.

We soon found that the different parts of the renal tubule, and more especially of Bowman's capsule and the glomerulus, varied considerably in size in different animals, so that it is necessary in making comparisons to use only, in the first instance, opposite kidneys in the same animal. Hence, our series of experiments comprises each possible combination in the above-named types of experiments.

All our experiments were performed upon cats anæsthetised with a mixture of chloroform and ether.

In all experiments, the kidney was removed and fixed in the following way. It was first carefully freed from subperitoneal fat, and a ligature then tied tightly around the pedicle close to the hilum. A second ligature was next tied around the pedicle a little nearer the aorta, and the pedicle divided between the ligatures. The object of ligaturing the pedicle was to keep the urine within the tubules, and as far as possible in the position it occupied at the instant of ligature. The kidney was dropped intact into a beaker of 20-per-cent. formalin made up with 0·9 per cent. NaCl. The beaker and solution had previously been weighed, and it was now weighed a second time, giving the weight of the kidney. At the end of an hour, the kidney was sliced into thin sections, fixation in formalin completed, and the pieces imbedded and sections prepared. The following measurements were then taken:—

1. An equatorial diameter of the capsule at right angles to the polar diameter.

2. The polar diameter, *i.e.* one passing through the point of entrance of the blood-vessels.

3. The greatest distance between the glomerulus and the capsule if the two were not in contact.

4. The maximal diameter of a typical proximal convoluted tubule.

5. The diameter of its lumen.

6 and 7. Similar measurements of a typical section of the distal convoluted tubule.

The glomeruli measured were taken at random, care being exercised only to measure those in which the section passed centrally. This was generally fairly easy to attain by taking those which showed the point of entrance of the blood-vessel into the glomerulus. From these measurements, calculations were made of the approximate volumes of the capsule and the glomerulus respectively. To obtain these, we regarded the capsule as equal in volume

to a sphere whose diameter was the mean of the two diameters of the capsule. The figures representing volumes given in this paper were obtained by cubing the mean radius of the capsule expressed in microns, and dividing it by 1000. Hence, to convert the figures into cubic millimetres, they must be multiplied by $4{\cdot}2 \times 10^{-6}$. The glomerulus was also compared to a sphere, whose diameter was the diameter of the capsule minus the maximum space between the glomerular surface and the capsular surface. The difference between the two volumes thus ascertained gives us an approximate estimate of the volume of the fluid contained within the capsule.

In measuring the tubules a section of a proximal convoluted tubule lying near to the glomerulus was selected, and that section of the distal convoluted tubule which lies close to the point of entrance of the vessels into the glomerulus. Hence the proximal tubule probably belonged to the glomerulus measured, and the distal tubule certainly did so belong.

I. *Comparison between a Resting and an Active Kidney.*

A. *The Glomerulus and Capsule.*—There are always marked differences between a resting and an active glomerulus. A resting glomerulus appears to be made up of a dense tissue closely packed with nuclei (fig. 1). The glomerular surface always lies in contact with the capsule wall, and the whole structure is usually irregularly quadrangular in outline. After activity the glomerulus stands away clearly from the capsule. The outline of the glomerulus is lobular, and in structure it is much looser than the resting glomerulus (fig. 2). It also appears to be filled with large vacuole-like spaces approximately circular in section. The nuclei are well separated. As a rule the number of blood corpuscles contained in the glomerular vessels is quite small, far fewer than in the resting glomerulus. This we think may be due to the expulsion of the blood from the capillary loops after excision of the kidney, or to *post-mortem* laking of the corpuscles. The latter may be produced by the diffusion of water from the capsule through the walls of the capillary loops after the epithelial cells have died, and before the fixative has had time to act upon them. This would account for the very characteristic vacuolated appearance of the glomeruli already alluded to.

We were never able to keep the blood in a kidney that was excised at the height of activity. At the instant of excision such a kidney is hard and tense, and instantly becomes soft when the first ligature is tied round the pedicle. This is even the case though the vein be first ligatured, and though the kidney may have been separated from its surrounding tissues before the diuretic was administered in order to give ample time for closure of the

many small vessels passing through the Capsule. Even then there is a distinct escape of blood through the Capsule, and the cortex rapidly pales in colour as the tension falls. The greater the tension at the instant of ligature, the greater is this paling of the cortex, and the sections of such kidneys may show but traces of blood in any of the capillaries, and but little in the veins.

The change in the shape of Bowman's capsule when the kidney becomes active is very distinctive. It becomes circular or elliptic in section, and there is always fluid between the glomerulus and the capsule wall. In many instances we have noted one other highly suggestive appearance. This is that the first portion of the proximal tubule has, in cases in which a free diuresis was established, been distended so as to appear almost a part of the capsule wall. An instance of this is illustrated in fig. 3. It is a very clear indication that the capsule and the first part of the convoluted tubule have been subjected to a high internal pressure. There are further indications, moreover, that the capsule has been distended to a size much larger than it appears in the section after fixation. The action of a high intracapsular pressure also adequately explains the change of shape from irregularly quadrangular to spheroidal or ellipsoidal.

B. *The Tubules.*—The contrast between the tubules at rest and after they have been in activity is just as striking, and in some particulars has already been described by several observers. In this paper we deal entirely with changes in the total diameter and in the lumen of the tubules, and, moreover, restrict our attention for the most part to the two convoluted tubules.

The magnitude of these several changes is brought out by the following measurements taken from Experiment 10. The measurements are in microns, and each is the mean of 10 measurements:—

Expt. 10.—R. kidney resting. L. kidney free.

	R. μ.	L. μ.
Glomeruli and capsules—		
Equatorial diameter	108·4	144·0
Polar diameter	78·4	103·6
Space	3·0	23·8
Hence		
Mean diameter capsule	93·4	123·8
" " glomerulus	90·4	100·0
Approximate volume capsule	102	237
" " glomerulus	92	125
" " fluid	10	112

Convoluted tubules—

Proximal.	External diameter ..	41·4	41·4
	Lumen	0·0	17·6
Distal.	External diameter ...	21·2	32·4
	Lumen	7·2	20·6

	grm.
Weight of R. kidney	10·9
" L. kidney	16·2

These figures show most clearly how extensive a change in size of the different parts of the renal tubule occurs when it is thrown into activity. Thus the capacity of the capsule is more than doubled (to 232 per cent.), chiefly because of the very large accumulation of fluid which has been secreted. The glomerulus is, however, increased to 136 per cent. of the volume of the glomerulus at rest. The differences are in reality still more marked, for a glomerulus actually at rest has no space between the glomerulus and the capsule wall, whereas in the right kidney of this animal no less than 7 of the 10 capsules measured contained fluid, though but small in amount.

We may conclude, then, that both Bowman's capsule and the glomerulus are distensible structures, and, further, that during activity the glomerulus does not remain in contact with the capsule wall, all of which strongly opposes the filtration theory of glomerular activity. These two conclusions are confirmed by every experiment we have performed.

When we turn to the measurements of the tubules the changes are equally striking. The external diameter of the proximal tubule is usually unaltered, but, whereas the resting tubule has no lumen, the tubule after action has a large lumen (43 per cent. of the total diameter). With the distal convoluted tubule the case is somewhat different. The total diameter is markedly increased (to 153 per cent.). The lumen of the resting tubule is 34 per cent., but that of the active tubule 64 per cent. of the total diameter of the tubule. Also, the lumen of the active tubule is 2·86 times greater than that of the resting. Apparently, then, the basement membrane of the proximal convoluted tubule is practically inextensible with the forces at play in this instance, whereas that of the distal convoluted tubule is extensible. In both tubules the cells are distinctly flattened against the basement membrane as a result of activity.

II. *Comparison between a Resting and a Decapsulated Kidney.*

The measurements obtained in an experiment of this character (Experiment 11) were as follows:—

Expt. 11.—R. kidney, resting. L. kidney, decapsulated and secreting freely.

		R.	L.
		μ	μ
	Glomeruli and capsules—		
	Equatorial diameter .. .	100·4	112·0
	Polar diameter	73·6	95·2
	Space	3·0	14·6
Hence			
	Mean diameter capsule	87·0	103·6
	" " glomerulus	84·0	89·0
	Approximate volume capsule......	82	139
	" " glomerulus	74	88
	" " fluid	8	51
	Convoluted tubules—		
	Proximal. External diameter ...	46·0	42·0
	Lumen.................	1·4	19·4
	Distal. External diameter ...	24·0	28·0
	Lumen	10·8	17·6

	grm.
Weight of R. kidney	8·4
" L. kidney	10·6

In this experiment the changes are entirely in the same direction as in the preceding, and the magnitude of the various changes is also approximately the same. If anything, the free kidney in the preceding experiment showed rather greater changes in comparison to the resting than did the decapsulated kidney of this experiment. The difference is, however, accounted for by the fact that the diuresis in Experiment 10 was greater than in Experiment 11.

The increase in volume of the capsule is to 170 per cent., of the glomerulus to 119 per cent. One notable difference is that in this experiment the external diameter of the proximal convoluted tubule was less after diuresis than when at rest.

III. *Comparison of a Free Kidney with a Free Decapsulated Kidney.*

Expt. 3.—R. kidney free. L. kidney free and decapsulated.

	R.	L.
	μ.	μ.
Glomeruli and capsules—		
Equatorial diameter	135·2	142·4
Polar diameter	100·8	112·0
Space	15·2	20·6

Hence

Mean diameter capsule	118·0	127·1
" " glomerulus .	100·8	106·5
Approximate volume capsule......	205	257
" " glomerulus	128	151
" " fluid.........	77	106

Convoluted tubules—

Proximal.	External diameter .	44·8	48·0
	Lumen	13·0	19·8
Distal.	External diameter . .	33·2	39·2
	Lumen	24·8	29·2

		grm.
Weight of	R. kidney.........	20·6
"	L. kidney.........	19·4

The two kidneys show the general changes of a diuresis in a well-marked manner. The experiment further shows that the effect of decapsulation is to cause a relatively greater expansion of both capsule and glomerulus. Also, the capsule is not so well emptied as in the normally active kidney. The difference in the dilatation of the convoluted tubules is again in favour of the decapsulated kidney. This is particularly seen with regard to the lumen of the proximal convoluted tubule. Whereas the ratio of the external diameter of the first convoluted tubule of the decapsulated kidney to that of the free kidney is 1 to 1·07, the ratio of the lumina is 1 to 1·53.

Hence we may conclude that decapsulation results in an increased distension of all the cortical parts of the kidney tubule when it is thrown into activity.

In the next group of experiments one of the kidneys was obstructed. The group comprises three comparisons.

IV. *Comparison of a Resting Kidney with an Obstructed Kidney.*

Expt. 12.—R. kidney resting. L. kidney obstructed.

	R.	L.
	μ.	μ.
Glomeruli and capsules—		
Equatorial diameter	98·4	130·4
Polar diameter	76·0	111·2
Space	1·2	24·8

Hence

Mean diameter capsule		87·2	120·8
" " glomerulus		86·0	96·0
Approximate volume capsule		83	220
" " glomerulus		80	111
" " fluid		3	109
Convoluted tubules—			
Proximal.	External diameter	44·0	42·8
	Lumen	0·0	10·4
Distal.	External diameter	25·4	31·8
	Lumen	11·0	21·8

	grm.
Weight of R. kidney	7·7
" L. kidney	10·9

The general changes are in the same direction as before. Perhaps the most marked difference between this and the previous kidneys examined is the large volume of fluid contained within the capsule, and the relatively small size of the glomerulus. Again, we note that there is no change in the external diameter of the proximal convoluted tubule, whereas the distal is extended to 125 per cent. of its resting diameter. As illustrated by the lumina, a very considerable volume of urine is collected within the tubules, particularly in the distal tubule.

V. *Comparison of a Free Kidney with an Obstructed Kidney.*

Expt. 6.—L. kidney free. R. kidney obstructed.

	R.	L.
	μ.	μ.
Glomeruli and capsules—		
Equatorial diameter	99·6	110·8
Polar diameter	77·2	100·0
Space	6·2	16·0

Hence

	R.	L.
Mean diameter capsule	88·4	105·4
" " glomerulus	82·2	89·4
Approximate volume capsule	86	146
" " glomerulus	69	89
" " fluid	17	57

Convoluted tubules—			
Proximal.	External diameter ...	39·2	39·4
	Lumen	6·6	14·0
Distal.	External diameter ...	22·8	28·2
	Lumen ...	12·6	18·4

	grm.
Weight of L. kidney ...	13·5
„ R. kidney ...	15·3

This experiment shows quite clearly the great effect of obstruction upon the distension of the capsule and accumulation of fluid within the capsule. Obstruction also causes a distinct further dilatation of the distal convoluted tubule, and an increase in the lumina of both parts of the tubule.

VI. *Comparison of a Free Decapsulated Kidney with an Obstructed Kidney.*

Expt. 7.—R. kidney decapsulated. L. kidney obstructed.

			R.	L.
			μ.	μ
	Glomeruli and capsules—			
	Equatorial diameter ...		121·2	130·4
	Polar diameter ...		102·0	111·2
	Space ...		9·8	20·0
Hence				
	Mean diameter capsule ...		111·6	120·8
	„ „ glomerulus ...		101·8	100·8
	Approximate volume capsule ...		174	220
	„ „ glomerulus		132	128
	„ „ fluid ...		42	92
	Convoluted tubules—			
	Proximal.	External diameter ...	42·0	41·4
		Lumen ...	15·4	17·6
	Distal.	External diameter ...	28·6	31·0
		Lumen ...	20·4	21·2

	grm.
Weight of R. kidney ...	10·7
„ L. kidney ...	11·0

The results of the measurements in this experiment show that obstruction of the ureter results in an increased expansion of the capsule of the obstructed, as compared to that of the free active kidney; this is entirely due to a greater accumulation of fluid within it. The convoluted tubules

show corresponding differences. The effect as before is mainly felt in the distal tubule, which shows a somewhat greater expansion. The lumina in the proximal tubules are greater in the obstructed kidney than in the free kidney. In this experiment the blood-pressure was rather low, but the diuresis good.

In all these obstructed kidneys the effect upon the medulla is very marked. Not only is the pelvis of the kidney greatly distended, but the pyramid is driven back towards the cortex, and appears very much shrunken. We have often seen it so contracted as to appear only about a quarter or less of its normal size. In the sections the collecting tubules are flattened and empty, the loops of Henle, however, contain fluid, and often appear to be about the same size as in the normal active kidney. The appearance of the pyramids is so characteristic that one can at once decide whether or no the ureter of that kidney had been obstructed in the experiment.

The last group of experiments comprises a comparison of various kidneys with a kidney which was both obstructed and decapsulated.

VII. *Comparison of a Resting Kidney with a Decapsulated and Obstructed Kidney.*

Expt. 13.—R. kidney resting. L. kidney decapsulated and obstructed.

		R. μ.	L. μ.
	Glomeruli and capsules—		
	Equatorial diameter	110·4	128·0
	Polar diameter	79·6	110·8
	Space	3·4	21·2
Hence			
	Mean diameter capsule	95·0	119·4
	" " glomerulus	91·6	98·2
	Approximate volume capsule	107	213
	" " glomerulus	96	118
	" " fluid	11	95
	Convoluted tubules—		
	Proximal. External diameter	46·0	49·6
	Lumen	0·0	26·4
	Distal. External diameter	21·8	34·4
	Lumen	10·6	24·4

	grm.
Weight of R. kidney	14·5
" L. kidney	19·3

An examination of the figures brings out an enormous increase in the size of the capsules, due chiefly to the increase in the amount of the fluid contained. The effect upon the convoluted tubules is again most marked. Otherwise the figures require no further comment.

The right kidney was not completely at rest, as was indicated by the microscopic appearance of the glomeruli. In every instance there was fluid between the glomerulus and the capsule.

VIII. *Comparison of a Free Kidney with a Decapsulated and Obstructed Kidney.*

Expt. 1.—R. kidney free. L. kidney decapsulated and obstructed.

		R. μ.	L. μ.
Glomeruli and capsules—			
	Equatorial diameter	135·6	143·6
	Polar diameter	106·8	125·6
	Space	23·8	31·6
Hence			
	Mean diameter capsule	121·2	134·6
	" " glomerulus	97·4	103·0
	Approximate volume capsule	223	305
	" " glomerulus	116	137
	" " fluid	107	168
Convoluted tubules—			
Proximal.	External diameter	48·2	51·4
	Lumen	13·2	24·0
Distal.	External diameter	38·6	39·8
	Lumen	29·0	30·8

The general result of the experiment shows that the glomeruli and convoluted tubules are more distended in the decapsulated and obstructed kidney than in the free kidney. In this instance the volume of the capsules became enormous, with only a slight increase in the volume of the glomeruli. We would emphasise the very great size of the lumen of the proximal convoluted tubule.

Expt. 4.—R. kidney free. L. kidney decapsulated and obstructed.

		R. μ.	L. μ.
Glomeruli and capsules—			
	Equatorial diameter	137·6	152·4
	Polar diameter	112·4	122·4
	Space	10·4	22·0

Hence

		L.	R.
Mean diameter capsule		125·0	137·4
" " glomerulus		114·6	115·4
Approximate volume capsule		244	324
" " glomerulus		188	192
" " fluid		56	132
Convoluted tubules—			
Proximal.	External diameter	45·6	43·4
	Lumen	15·2	22·8
Distal.	External diameter	27·8	29·4
	Lumen	15·8	21·2

	grm.
Weight of R. kidney	16·5
" L. kidney	18·7

The results obtained in this experiment in every way confirm those shown in the previous experiment.

IX. *Comparison of a Decapsulated Kidney with a Decapsulated and Obstructed Kidney.*

Expt. 2.—L. kidney decapsulated. R. kidney decapsulated and obstructed.

		L. μ.	R. μ.
Glomeruli and capsules—			
Equatorial diameter		142·4	161·2
Polar diameter		122·4	129·2
Space		6·2	12·4
Hence			
Mean diameter capsule		132·4	145·2
" " glomerulus		126·2	132·8
Approximate volume capsule		290	383
" " glomerulus		251	293
" " fluid		39	90
Convoluted tubules—			
Proximal.	External diameter	47·4	47·2
	Lumen	12·4	19·2
Distal.	External diameter	30·4	36·4
	Lumen	18·8	24·2

	grm.
Weight of L. kidney	13·6
" R. kidney	16·6

The results of the experiment are again very decisive, a notable point being the large volume the glomeruli in both kidneys. We would again point out that the main effect upon the convoluted tubules is seen in the distal tubules.

Expt. 5.—R. kidney decapsulated. L. kidney decapsulated and obstructed.

		R. μ.	L. μ.
Glomeruli and capsules—			
Equatorial diameter		144·8	151·6
Polar diameter		111·6	136·8
Space		24·0	37·6
Hence			
Mean diameter capsule		128·2	144·2
" " glomerulus		104·2	106
Approximate volume capsule		263	375
" " glomerulus		141	151
" " fluid		122	224
Convoluted tubules—			
Proximal.	External diameter	45·6	51·0
	Lumen	20·8	25·2
Distal.	External diameter	34·0	42·0
	Lumen	23·0	30·6

	grm.
Weight of R. kidney	17·6
" L. kidney	18·0

The figures are in agreement with those of the preceding experiment, with the exception that the volume of the glomeruli in this instance is small. In Experiment 2 the blood-pressure was low (83 mm. Hg) and the diuresis moderate, while in Experiment 5 the blood-pressure was high (130 mm. Hg) and the flow of urine rapid.

X. *Comparison of an Obstructed Kidney with a Decapsulated and Obstructed Kidney.*

Expt. 8.—L. kidney obstructed. R. kidney decapsulated and obstructed.

	L. μ.	R. μ.
Glomeruli and capsules—		
Equatorial diameter	109·2	108·0
Polar diameter	95·6	95·2
Space	11·8	9·2

Hence

Mean diameter capsule		102·4	101·6
" " glomerulus		90·6	92·4
Approximate volume capsule		134	131
" " glomerulus		93	99
" " fluid		41	32
Convoluted tubules—			
Proximal.	External diameter	40·4	41·4
	Lumen	17·8	18·2
Distal.	External diameter	25·4	29·6
	Lumen	17·2	21·0

	grm.
Weight of R. kidney	15·8
" L. kidney	15·8

In this experiment the blood-pressure was low and the flow of urine small, and with it again the volume of fluid in the capsule is small. In general, it confirms the result of the preceding experiments. Decapsulation combined with obstruction produces a greater distension of the tubules than obstruction alone. With a more abundant diuresis than occurred in this experiment a similar result is found in the capsules and glomeruli.

In the following tables we collect the results obtained in our thirteen experiments. In the first we give the means of the approximate volumes of Bowman's capsule, glomerulus and fluid, and in the second the ratios of these to the similar structures in the resting kidney.

We would not lay much stress upon comparisons between these figures, except when the differences are very marked. There are so many varying factors upon which the actual magnitudes of the measurements depend that to do so would lead to erroneous conclusions. Thus, the results vary with the blood-pressure, with the degree of diuresis established, the duration of the diuresis, and especially with the degree of extensibility of the kidney Capsule, and of the general renal tissues, both of which we know to vary greatly in different animals. Table II, however, shows very decisively the enormous changes in size of the glomerulus and capsule caused by active secretion of water, and more especially in the very great accumulation of water within the capsule during activity. All these results are of the highest importance in disproving the possibility of filtration at the glomerular surface.

Table I.

	Volume Bowman's capsule.	Volume glomerulus.	Volume fluid.	No. of experiments.
Resting	94	85	9	4
Active free	227	137	90	4
„ decapsulated	229	162	67	5
„ obstructed	196	136	60	3
„ decapsulated and obstructed	277	157	120	6

Table II.—Ratios.

	Bowman's capsule.	Glomerulus.	Fluid.
Resting	1 ·00	1 ·00	1 ·00
Active free	2 ·42	1 ·61	10 ·00
„ decapsulated	2 ·44	1 ·91	7 ·44
„ obstructed	2 ·09	1 ·60	6 ·67
„ decapsulated and obstructed	2 ·95	1 ·85	13 ·34

In Tables III and IV we give similar figures for the convoluted tubules.

Table III.

	Proximal.		Distal.	
	External diameter.	Lumen.	External diameter.	Lumen.
Resting	44 ·4	0 ·4	23 ·4	9 ·9
Active free	45 ·0	14 ·8	33 ·0	22 ·6
„ decapsulated	46 ·0	17 ·3	33 ·2	22 ·2
„ obstructed	42 ·0	19 ·0	29 ·3	20 ·3
„ decapsulated and obstructed	47 ·3	22 ·6	35 ·3	25 ·4

Table IV.—Ratios.

	Proximal.		Distal.	
	External diameter.	Lumen.	External diameter.	Lumen.
Resting	1 ·00	1 ·00	1 ·00	1 ·00
Active free	1 ·01	37 ·00	1 ·41	2 ·28
„ decapsulated	1 ·04	43 ·25	1 ·42	2 ·24
„ obstructed	0 ·95	47 ·50	1 ·25	2 ·05
„ decapsulated and obstructed	1 ·07	56 ·50	1 ·51	2 ·57

These two tables bring out the following points:—

(1) The external diameter of the proximal convoluted tubule does not change on activity;

(2) A large lumen is developed in this tubule during diuresis. It varies with the degree of diuresis, and is markedly increased by obstruction of the ureter. Taking the average of all our observations it amounts to nearly 40 per cent. of the total diameter of the tubule;

(3) The distal convoluted tubule is expanded considerably (from 140 to 150 per cent. of its mean at rest); and

(4) The lumen, of considerable size (42·3 per cent. of the total diameter) even in a resting kidney, is more than doubled, and becomes 69·2 per cent of the total diameter.

We may conclude, then, that the first convoluted tubule, *i.e.* that portion which is subjected to the highest internal pressure, is relatively inextensible transversely. The second convoluted tubule, on the other hand, is transversely extensible. From a further examination of our sections, we judge that the proximal convoluted tubules do indicate an extension in the longitudinal direction, but our present methods do not allow us to state this decisively.* All the results indicate that an internal pressure has existed during diuresis.

Conclusions.

Measurements of the diameters of the various portions of the renal tubule in the cat, when at rest and after diuresis under various conditions, show that Bowman's capsule, the glomerulus, and the second convoluted tubule are extensible structures, and are expanded during diuresis. The glomerulus leaves the capsule wall, a considerable accumulation of secretion being found between them. The lumina of all parts of the tubule become greatly enlarged.

All the appearances found are explained as resulting from the action of a high pressure in the fluid secreted by the glomerular epithelium, and are all in accordance with the propulsor theory of the action of the glomerulus.

* If we may make the assumption that the volume of the cells of the convoluted tubule does not alter during diuresis, then the magnitude of the surface areas of the cells in a transverse section of the tubule gives us an indication of any change in length. If, for this purpose, we examine the results of Experiments 10, 11, 12, and 13, where we have direct comparisons of active with resting kidneys, we find that in all instances the proximal convoluted tubules are markedly stretched longitudinally. In Experiments 10 and 13 there is considerable shortening of the distal convoluted tubules, and in Experiments 11 and 12 slight shortening. In Experiment 10 and 13 the blood-pressure was high and the diuresis good. In Experiments 11 and 12 the blood-pressure was lower and the diuresis only moderate. Hence it would appear that, with a high internal pressure, this portion of the tubule is shortened, *i.e.* tends towards the spherical shape.

DESCRIPTION OF PLATE.

Fig. 1. Microphotograph of Cortex of Dog's Kidney at Rest. × 500.

Fig. 2.—Microphotograph of Cortex of Opposite Kidney after Activity. × 500.

Fig. 3.—Cat's Kidney. Drawing of glomerulus and tubules after activity, showing dilatation of neck of tubule. × 500.

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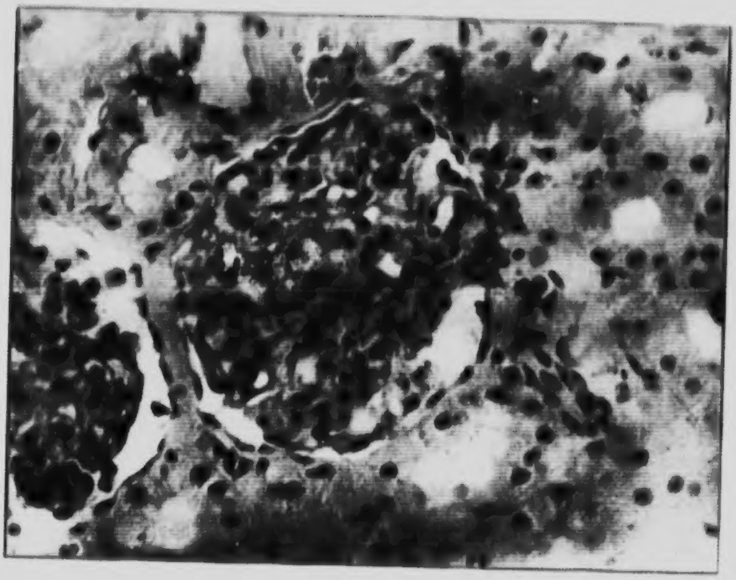

FIG. 1.

FIG. 2.

Fig. 3.

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